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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KRUSE, DAVID H

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1638

DATE MAILED: 10/24/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/680,858	BEETHAM ET AL.
	Examiner David H Kruse	Art Unit 1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 07 May 2002.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-32 is/are pending in the application.

4a) Of the above claim(s) 1-23 and 25-27 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 24 and 28-32 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .	6) <input type="checkbox"/> Other: _____ .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group V, claim 24 in Paper No. 9, filed 7 May 2002 is acknowledged. The traversal is on the ground(s) that the methods of making and the intermediate products should be examined together and that the end products, the mutated plants, are restrictable. This is not found persuasive because the product of Group V can be made using various methods, such as those in the instant claims, in addition to other methods not in the claims such as lipofection and biolistic methods.

The requirement is still deemed proper and is therefore made FINAL.

2. The Examiner has additionally grouped new claims 28-32 with the elected claim 24. The mutated plant microspore of claims 30-32 is considered an inherent subset of the elected invention.

3. Claims 1-22 and 25-27 are withdrawn from further consideration pursuant to 37 CFR § 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

4. This application contains claim 1-22 and 25-27 drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR § 1.144). See MPEP § 821.01.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if

one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17(i).

Amendment

6. The Amendment filed 7 May 2002 does not comply with 37 CFR 1.121(c)(1)(i) that requires a clean version of the claim to be submitted in addition to a markup version. Accordingly the amendment to claim 5 has not been entered into the application.

7. The amendment filed 7 May 2002 has been entered in part, specifically new claims 26-32 have been entered into the instant application.

Information Disclosure Statement

8. The information disclosure statement (IDS) submitted on 10 September 2001 has been considered by the examiner. A copy is attached hereto.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 24 and 28-32 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a plant microspore comprising any mixed duplex oligonucleotide and any mutated plant microspore, which comprises any genomic mutation wherein the genomic mutation was accomplished by introducing a mixed duplex oligonucleotide into the plant microspore.

Applicant describes mixed duplex oligonucleotides for mutating genomic tobacco ALS-1, ALS-2 and putrecene N-methyltransferase; *Arabidopsis* PAT4, PAT3, ATFAD2/217; and Canola AHAS3 sequences (see pages 24, 30 and 31 of the specification).

Applicant does not describe other mixed duplex oligonucleotides for mutating genomic sequences in a plant microspore, nor does Applicant describe mixed duplex oligonucleotides for use in *Brassica* plants other than *Arabidopsis*.

Hence, it is unclear from the instant specification that Applicant was in possession of the invention as broadly claimed.

11. Claims 24 and 28-32 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims a plant microspore comprising any mixed duplex oligonucleotide and any mutated plant microspore, which comprises any genomic mutation wherein the genomic mutation was accomplished by introducing a mixed duplex oligonucleotide into the plant microspore.

Applicant teaches mixed duplex oligonucleotides for mutating genomic tobacco ALS-1, ALS-2 and putrecene N-methyltransferase; *Arabidopsis* PAT4, PAT3, ATFAD2/217; and Canola AHAS3 sequences (see pages 24, 30 and 31 of the specification).

Applicant does not teach other mixed duplex oligonucleotides for mutating genomic sequences in a plant microspore, nor does Applicant teach mixed duplex oligonucleotides for use in *Brassica* plants other than *Arabidopsis*. In addition, the examples in the specification directed to introducing mixed duplex oligonucleotides for mutating genomic sequences appear prophetic in the instant case.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

In the instant case, Applicant has provided limited guidance for how to make and use the invention within the breadth of the claims. The examples in the instant specification appear to be prophetic. The nature of the invention is such that one of skill in the art must determine the native sequence of the targeted genomic sequence in order to design a mixed duplex oligonucleotide in order to make the claimed invention. In addition the art teaches that the art to which the instant claims are directed was, at

the time of the instant invention, unpredictable as to how to make and use the invention as broadly claimed. Hohn *et al* (1999, Proc. Natl. Acad. Sci. USA 96:8321-8323) teaches that not all mixed duplex oligonucleotides will produce the intended mutation and that there appears to be a high degree of variability between plant species in how a plant responds to a mixed duplex oligonucleotide (see paragraph spanning columns on page 8323). Hence, given the limited guidance by Applicant, the nature of the invention, and the teachings of the art, it would have required undue trial and error experimentation by one of skill in the art at the time of the invention to make and use the invention as broadly claimed.

12. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claim 30 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. At line 1, the phrase "comprises a microspore" is indefinite because it is unclear how a plant microspore can comprise itself, hence it is unclear what the metes and bounds of the claimed invention are. It appears that the phrase "a microspore that has" should be deleted.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

15. Claims 24 and 28-32 are rejected under 35 U.S.C. § 102(a) as anticipated by Hawkes *et al* (WO 98/54330, published 3 December 1998, priority date 28 May 1997).

Hawks discloses a maize pollen (microspore) comprising a mixed duplex oligonucleotide and a mutant plant microspore comprising a genomic mutation for herbicide resistance (see page 12, 1st paragraph). Hawks discloses that the plant cell, such as a microspore, to which the methods are applied may be a cell of a plant selected from cabbage (*Brassica oleracea*) or oilseed rape (*B. napus* or *B. juncea*) (see page 3, lines 13-18). Hence, Hawks also inherently discloses a Brassica microspore comprising a mixed duplex oligonucleotide or a mutant Brassica microspore.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 24 and 28-32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kmiec (US Patent 5,731,181, filed 17 June 1996) in view of Fennell *et al* (1992, Plant Cell Reports 11:567-570).

Kmiec teaches a method of introducing an alteration in a target sequence of the genome of a plant cell comprising introducing a mixed duplex oligonucleotide into a plant cell (see claims 30-32). Kmiec also teaches that the mixed duplex oligonucleotide can be introduced into a cell using a wide variety of techniques known in the art at the

time of Applicant's invention including electroporation and liposome mediated fusion (see column 1, lines 29-33).

Kmiec does not specifically disclose a method for introducing mixed duplex oligonucleotides into plant microspores.

Fennell teaches methods of introducing DNA into plant microspores, specifically maize microspores, using both electroporation and PEG (see entire reference). Fennell also teaches that using microspores has the advantage as useful for producing haploid plants that can be used to produce homozygous diploids (see page 567, right column, end of Introduction).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the teachings of Kmiec to produce microspores comprising a mixed duplex oligonucleotide and mutated plant microspores therefrom using the method of Fennell. One of ordinary skill in the art at the time of Applicant's invention would have had a reasonable expectation of success given the success of Fennell in transferring DNA into maize microspores. The *Brassica* species microspores of the instant claims would have been considered function equivalents to the maize microspores of Fennell, and would not have lead to the teaching of unexpected results, without evidence to the contrary.

18. Claims 24 and 28-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kmiec (US Patent 5,731,181, filed 17 June 1996) in view of Saunders *et al* (US Patent 5,629,183, published 13 May 1997).

The teachings of Kmiec are discussed above.

Kmiec does not specifically disclose a method for introducing mixed duplex oligonucleotides into plant microspores.

Saunders teaches a method of introducing DNA into pollen grains of plants by electroporation to effect a modification in the plant's genome (see claim 1). Saunders also teaches that the method is applicable to plants of all species (see column 2, lines 15-21).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the teachings of Kmiec to produce microspores comprising a mixed duplex oligonucleotide and mutated plant microspores therefrom using the method of Saunders. One of ordinary skill in the art at the time of Applicant's invention would have had a reasonable expectation of success given the success of Saunders in transferring DNA into tobacco microspores (see claim 10). The Brassica species microspores of the instant claims would have been considered function equivalents to the tobacco microspores of Saunders, and would not have lead to the teaching of unexpected results, without evidence to the contrary.

Conclusion

19. No claims are allowed.
20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Kim Davis whose telephone number is (703) 305-3015.



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David H. Kruse, Ph.D.
17 October 2002